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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/705,302	11/02/2000	Kurt Berlin	81587	4345

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EXAMINER

LY, CHEYNE D

ART UNIT	PAPER NUMBER
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1631

14

DATE MAILED: 08/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/705,302

Applicant(s)

BERLIN ET AL.

Examiner

Cheyne D Ly

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 19, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-15,17,19-28,30-40 and 42-50 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-15, 17, 19-28, 30-40, and 42-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' arguments in Paper No. 13, filed May 19, 2003, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. Applicants' cancellation of claims 2, 16, 18, 29, and 41 has been acknowledged.
3. Claims 1, 3-15, 17, 19-28, 30-40, and 42-50 are examined on the merits.

Response to Arguments

4. Claims 1, 3-15, 17, 19-28, 30-40, and 42-50 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
5. This rejection is maintained with respect to claims 1, 3-15, 17, 19-28, 30-40, and 42-50, as recited in the previous office action Paper No. 11, mailed November 14, 2002.
6. It is reiterated that the Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art,

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(7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

7. Specific to the limitation of "expert rules", Applicants argue the instant specification provides adequate guidance and direction to enable the person of ordinary skill in the art to practice the invention without undue experimentation. Applicants cite the disclosure of the advantages of a "pluralistic approach" over the disadvantage of the state of the art for analysis of cancer cells; linkage between methylation and expression with respect to a disease (pages 2-3 and 11-14) is adequate enablement disclosure. It is noted that cited advantages and disadvantages is useful, however, they do not help Applicants overcome the lack of enablement issue of the instant application. Further, Applicants disclose "a person of ordinary skill in the art would be taught and guided to develop expert rules by...putting together the above information in a "complex scenario approach." The above pointed to support and arguments have been fully considered and found to be unpersuasive for the reasons discussed below.

8. As stated by Applicants above, in order to practice the instant invention "a person of ordinary skill in the art would be taught and guided to develop expert rules by...putting together the above information in a "complex scenario approach." However, the Examiner has not been able to find any disclosure in the instant specification that would teach one of ordinary skill in the art to develop these expert rules. It is acknowledged that Applicants disclose a second knowledge base comprising a plurality of expert rules for selecting a

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therapeutic treatment regimen for the disease (page 17, lines 16-18). Further, Applicants disclose a knowledge base that has subjective rules, objective rules, and system-generated rules (page 45, lines 9-17) and how these rules have been developed. However, it is suggested by the instant specification that the expert rules knowledge base is different from the knowledge base comprising subjective rules, objective rules, and system-generated rules. Therefore, it is concluded that the instant specification does not provide sufficient guidance to one of ordinary skill in the art to develop these expert rules without undue experimentation.

9. Applicants further pointed to pages 5 to 6 of the instant specification to argue that “expert rules” are based on formal techniques and algorithmic approaches. It is acknowledged that Applicants discloses “a method which could classify cells and cell groups according to states.” However, the instant specification does not specify how the disclosed method is used to develop expert rules.

10. With respect to “selecting a type of disease or medical condition based on the methylation status...,” and “ranked listing of diseases [...] based on the information about the methylation status [...]” Applicants argue both terms do not mean that the selection has to be understood as an all-or-nothing selection and the selection will be made based on a variety of cut-off values that would result in a ranked listing of more or less disease states. However, the specification does not provide guidance as how these cut-off values are determined.

11. Further, Applicants argue the methylation data is used for determining different ranked listing of diseases and the quality of the ranked listings. Since the methylation data “should

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always be as good as possible,” there is no need to give certain parameter for the selection practice. However, the instant specification contradicts Applicants’ argument in regard to the quality of ranking by methylation data. The said methylation is not capable of reliably analyzing minute fragments from small sample quantities (page 9, lines 19-21); suggesting that not all methylation data are “as good as possible.” Therefore, one of ordinary skill in the art would need guidance and direction for selecting a type of disease or medical condition based on the methylation status; or generating a ranked listing based on the said methylation data.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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14. Claims 1, 4, and 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barry et al. (US PN 6081786) taken with Ben-Yehuda. (December 1997).

15. This rejection is maintained with respect to claims 1, 2, 4 and 6-13, as recited in the previous office action Paper No. 11, mailed November 14, 2002.

16. First, Applicants argue Barry et al. does not suggest the limitation of the diagnosis of an unknown disease (i.e. yet-to-be diagnosed) and Ben-Yehuda et al. does not suggest the limitation diagnosis of a disease.

17. Second, Applicants argue there is no basis for combining the references.

18. Third, Ben-Yehuda et al. suggests methylation method, which is of low sensitivity, despite the use of PCR. Further, Ben-Yehuda is silent about the inclusion of additional methylation analysis outside of *abl* in order to increase the accuracy of the diagnosis.

19. In regard to the above arguments, Applicants' arguments have been fully considered and found to be unpersuasive.

20. As directed to the first and third arguments above, the claims of the instant application do not limit the scope of the instant invention to the limitation of diagnosis of an unknown disease or a method with the highest sensitivity. It is acknowledged that Applicants discuss these topics in the instant specification. However, disclosures in the specification do not limit the scope of the claims.

21. Specific to the first argument, Ben-Yehuda et al. does not suggest the limitation the diagnosis of a disease. Diagnosis is the act or process of identifying or determining the nature and cause of a disease or injury through evaluation of patient history, examination, and review of laboratory data (Dictionary.com, page 1, ¶ 1). Ben-Yehuda et al. discloses a

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molecular follow-up of disease progression and interferon therapy in chronic myelocytic leukemia, which is consistent with the limitation of diagnosis as defined above.

22. Specific to the second argument, it is noted that the system of Barry et al. is directed to a general tool for selecting therapeutic treatment regimens, thus, suggesting the said system and method could be used for the selection of any therapeutic treatment regimen. Barry et al. discloses a system and method for the selection of therapeutic treatment regimens for treating patients (column 2, lines 47-51). While Ben-Yehuda et al. discloses a treatment regimen selection for patients with chronic myelocytic leukemia based on methylation status (Materials and Methods, Page 4919, Column 1 and 2). One of ordinary skill in the art would have been motivated to develop a tool for the selection therapeutic treatment regimens, as taught by Barry et al., based on methylation status, as taught by Ben-Yehuda et al.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to used a computer system for the selection of therapeutic treatment regimens based on methylation status as taught by Barry et al. and Ben-Yehuda et al.

CONCLUSION

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

24. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory

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period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

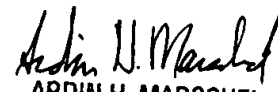
25. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

27. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

28. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
8/4/03


ARDIN H. MARSCHER
PRIMARY EXAMINER